REMARKS

Claims 108-134, 137-139, 142-160, 211-235, and 297-318 are pending and stand rejected. Claims 108-110, 129, 132, 152, 156, 159, 160, 211, and 232 have been amended. No new matter has been introduced. Reconsideration and allowance of Claims 108-134, 137-139, 142-160, 211-235, and 297-318 is respectfully requested.

The Objection to the Specification

The specification has been amended on page 29 to recite that FIGURES 45A and 45B are SEQ ID NO:23. The specification has also been amended to remove embedded hyperlinks as requested by the Examiner. Removal of the objection to the specification is respectfully requested.

The Objections to the Claims

Claims 129, 132, and 211 have been amended to correct the minor informalities noted by the Examiner. Removal of this ground of objection is respectfully requested.

The Rejection of Claims 108-134, 137-139, 142-158, 211-235, and 299-318 Under 35 U.S.C. § 101

Claims 108-134, 137-139, 142-158, 211-235, and 299-318 stand rejected under 35 U.S.C. § 101 based on non-statutory subject matter.

In order to facilitate prosecution, independent Claim 108 (from which Claims 109-134, 137-139, 142-158, 299-307, and 317 depend), has been amended to include the recitation "wherein step (B) is performed by a suitably programmed computer." Support for this

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

amendment is found in the specification as filed; for example, at page 12, line 5, to page 14, line 11.

Independent Claim 211 (from which Claims 212-235, 308-316, and 318 depend), has been amended to include the recitation "wherein at least one of steps (A) or (B) is performed by a suitably programmed computer." Support for this amendment is found in the specification as filed; for example, at page 12, line 5, to page 14, line 11.

Removal of this ground of rejection is respectfully requested.

The Rejection of Claims 109, 110, 121, 128-134, 137-139, 142-145, 147-148, 152, 154, 156-158, 223, 232, and 307 Under 35 U.S.C. § 112, Second Paragraph

Claims 109, 110, 121, 128-134, 137-139, 142-145, 147-148, 152, 154, 156-158, 223, 232, and 307 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

The Examiner has taken the view that the term "associated with" in Claims 109, 110, 119, 120, and 304 is a relative term which renders the claim indefinite. While not acquiescing with the Examiner's position, but in order to clarify the claimed invention, Claims 109 and 110 have been amended to replace the phrase "wherein each quantitative measurement in said plurality of quantitative measurements of said first trait is associated with an organism in said plurality of organisms," with the phrase "wherein each quantitative measurement in said plurality of quantitative measurements of said first trait is obtained from an organism in said plurality of organisms." Support for this amendment is found in the specification; for example, at page 18, line 30, to page 19, line 14.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

With regard to Claims 119, 120, and 304 it is noted that the meaning of the term "associated" in the context of the phrase "a complex phenotype associated with human disease," as recited in Claims 119 and 120, and in the context of the phrase "wherein said complex trait is associated with a high frequency of disease-causing alleles in said species," as recited in Claim 304, would be understood by those of skill in the art in view of the specification. For example, the specification at page 148, lines 16-26, describes association studies which test whether a disease and an allele show correlated occurrence across a population.

The Examiner has taken the view that the equations in Claims 152, 156, and 232 lack clarity.

Claim 152 has been amended to delete the term "=". Support for this amendment is found in the specification at page 8, lines 26-30.

Claim 156 has been amended to replace the term "Q." with the term "Q*". Support for this amendment is found in the specification at page 10, lines 1-15.

Claim 223 has been amended to correct antecedent basis and now recites "at least one organism in said plurality of organisms."

Claim 232 has been amended to delete one of "+" symbols. Support for this amendment is found in the specification at page 8, lines 26-30.

Removal of this ground of rejection of Claims 152, 156, 223, and 232, and dependent Claims 154 and 157-158 is respectfully requested.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

The Rejection of Claims 108-134, 137-139, 142-160, 211-235, and 297-318 Under 35 U.S.C. § 102(e) as Being Anticipated by U.S. Patent Publication No. 2006/0111849 (Schadt et al.)

Claims 108-134, 137-139, 142-160, 211-235, and 297-318 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent Publication No. 2006/0111849 (Schadt et al.). Applicants respectfully traverse this ground of rejection for at least the following reasons.

Claims 108-134, 137-139, and 142-160

While not acquiescing to the Examiner's position, but in order to facilitate prosecution, independent Claims 108 (from which Claims 109-134, 137-139, 142-158, 299-307, and 317 depend), 159, and 160 have been amended as follows.

Claim 108:

> A method for determining whether a first trait T_1 is causal for a second trait T_2 in a plurality of organisms of a species, the method comprising:
>
> (A) identifying one or more loci in the genome of said species, wherein each locus Q of said one or more loci is a site of colocalization for (i) a respective quantitative trait locus (QTL_1) that is genetically linked to a variation in the first trait T_1 across the plurality of organisms and (ii) a respective quantitative trait locus (QTL_2) that is genetically linked to a variation in the second trait T_2 across said plurality of organisms; and
>
> (B) determining whether said first trait T_1, is causal for said second trait T_2, comprising testing, for each respective locus Q of said one or more loci identified in step (A), whether (i) a genetic variation Q^* of said respective locus Q across said plurality of organisms and (ii) said

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

variation in said second trait T_2 across said plurality of organisms are correlated conditional on said variation in said first trait T_1 across said plurality of organisms,

wherein, when the genetic variation of (i) one or more loci *Q* tested in (B), and (ii) said variation in said second trait T_2 across said plurality of organisms are correlated conditional on said variation in said first trait T_1 across said plurality of organisms, said first trait T_1 is determined to be causal for said second trait T_2, wherein step (B) is performed by a suitably programmed computer.

Support for the amendment to step (B) of Claim 108 is found in the specification; for example, at page 17, lines 25-31.

Claim 159 has been amended and now recites:

A computer program product for use in conjunction with a computer system, the computer program product comprising a computer readable storage medium and a computer program mechanism embedded therein, the computer program mechanism comprising:

a T_1/T_2 overlap module that comprises instructions for identifying one or more loci in the genome of a species, wherein each locus *Q* of said one or more loci is a site of colocalization for (i) a respective quantitative trait locus (QTL_1) that is genetically linked to a variation in a first trait T_1 across a plurality of organisms in said species and (ii) a respective quantitative trait locus (QTL_2) that is genetically linked to a variation in a second trait T_2 across said plurality of organisms; and

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

a causality test module for determining whether said first trait T_1 is causal for said second trait T_2 that comprises instructions for testing, for one or more locus Q of said one or more loci, whether (i) a genotype random variable [[Q•]] Q* of the respective locus Q across the plurality of organisms and (ii) said variation in the second trait T_2 across the plurality of organisms are correlated conditional on the variation in said first trait T_1 across the plurality of organisms.

Support for the amendment to Claim 159 is found in the specification at page 13, line 21, to page 14, line 11; and page 17, lines 25-31.

Claim 160 has been amended and now recites:

A computer system comprising:

a central processing unit;

a memory, coupled to the central processing unit, the memory storing an Q_1/Q_2 overlap module and a causality test module; wherein

the T_1/T_2 overlap module comprises instructions for identifying one or more loci in the genome of a species, wherein each locus Q of said one or more loci is a site of colocalization for (i) a respective quantitative trait locus (QTL_1) that is genetically linked to a variation in the first trait T_1 across a plurality of organisms of said species and (ii) a respective quantitative trait locus (QTL_2) that is genetically linked to a variation in the second trait T_2 across said plurality of organisms; and

a causality test module for determining whether said first trait T_1 is causal for said second trait T_2 that comprises instructions for testing, for one or more loci Q in the at least one locus, whether (i) a genotype random

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

variable Q_* for the respective locus Q across the plurality of organisms and (ii) said variation in said second trait T_2 across said plurality of organisms are correlated conditional on the variation in the first trait T_1 across said plurality of organisms.

Support for the amendment to Claim 160 is found in the specification; for example, at page 13, line 21, to page 14, line 11; and page 17, lines 25-31.

It is noted that independent Claims 108, 159, and 160, as amended, are not anticipated by U.S. Patent Application Publication No. 2006/0111849 ("Schadt et al.") because Schadt et al. does not teach all the limitations of the claims, as amended. The claimed invention, as amended, is directed to methods for determining whether a first trait T_1 is causal for a second trait T_2. As described in the instant specification, the present invention provides a test to determine whether a first trait drives (is causal for) a second trait. See specification at page 17, lines 25-31. The cited reference Schadt et al. does not teach methods of determining causality as claimed. Rather, Schadt et al. is generally directed to methods for combining gene expression data with genetics data to determine whether the eQTL and the cQTL colocalize to the same locus in the genome of the species in order to elucidate biological pathways associated with traits. See Schadt et al. at paragraph [0017].

As further described in Schadt et al.

> Also, in some embodiments, gene expression data for multiple genes identified using the techniques described above are considered simultaneously using multivariate analysis <u>in order to verify that each of the genes is involved in the same biological pathway</u>. It is possible to have a plurality of genes having coregulated expression that actually represent unrelated biological pathways. The multivariate analysis of the present

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

invention is advantageous is such situations because the analysis can be used to determine whether a set of genes represents more than one biological pathway. [Schadt et al. at paragraph [0018] (emphasis added).]

It is further noted that Schadt et al. does not teach a method comprising the step of determining whether said first trait T_1, is causal for said second trait T_2, comprising testing whether (i) a genetic variation Q^* of said respective locus Q across said plurality of organisms and (ii) said variation in said second trait T_2 across said plurality of organisms are correlated conditional on said variation in said first trait T_1 across said plurality of organisms, wherein, when the genetic variation of (i) one or more loci Q tested in (B), and (ii) said variation in said second trait T_2 across said plurality of organisms are correlated conditional on said variation in said first trait T_1 across said plurality of organisms, said first trait T_1 is determined to be causal for said second trait T_2.

As described in the instant specification, "The aim of the causality test is to distinguish between the relationships that indicate a cellular constituent is causal for the clinical trait (scenarios 302, 308, and 310 of Fig. 3A) from those that are reactive to, or independent of the disease trait (scenarios 304 and 306, respectively, of Fig. 3A)." Specification at page 55, lines 16-19 (emphasis added). Therefore, it is demonstrated that Claims 108, 159, and 160, as amended, are not anticipated by Schadt et al.

Claims 211-235 and 297-318

Contrary to the Examiner's assertion, it is noted that independent Claims 211 and 297 are not anticipated by Schadt et al. because the cited reference does not disclose all the elements of the claimed invention. For example, Schadt et al. does not teach step C of Claims 211 and 297 which recites:

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

(C) quantifying a second coefficient of determination between (i) said genetic variation Q^* of said locus Q across all or a portion of said plurality of organisms and (ii) said variation in said first trait T_1 across all or a portion of said plurality of organisms, after conditioning on said variation in said second trait T_2 across all or a portion of said plurality of organisms, wherein said first trait T_1 is deemed to be causal for said second trait T_2 when said first coefficient of determination is other than zero and said second coefficient of determination cannot be distinguished from zero . . . .

It is further noted that Schadt et al. does not qualify as citable prior art under 35 U.S.C. § 103(a). Under 35 U.S.C. § 103(c)(1), a reference that qualifies as prior art only under § 102(e) cannot be used as a reference against the claimed invention if the subject matter of the reference and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person. Subject matter that would be prior art to the claimed invention and the claimed invention itself are considered to be "commonly owned" if the subject matter and the claimed invention are wholly owned by the same organization or business entity at the time the invention was made. See M.P.E.P. § 706.02(1)(2)(I).

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

STATEMENT OF COMMON OWNERSHIP UNDER 35 U.S.C. § 103(c)

U.S. Patent Application No. 10/523,143 (published as U.S. Patent Application Publication No. 2006/0111849) was, at the time the invention of U.S. Patent Application No. 10/567,282 was made, wholly owned by Merck and Co., Inc., of Rahway, New Jersey. The above statement is sufficient evidence to disqualify U.S. Patent Application No. 10/523,143 (Schadt et al.) from being used in a rejection under 35 U.S.C. § 103(a) against the claims of the instant application. See M.P.E.P. § 706.02(l)(2)(II).

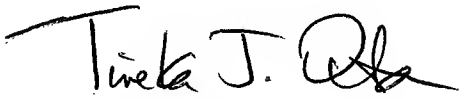
LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

CONCLUSION

Applicants believe that all of the pending claims are in condition for allowance. Reconsideration and favorable action are requested. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney at 206.695.1655.

Respectfully submitted,

CHRISTENSEN O'CONNOR
JOHNSON KINDNESS[PLLC]



Tineka J. Quinton
Registration No. 53,496
Direct Dial No. 206.695.1655

TJQ:jlg

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS[PLLC]
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100